(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 September 2000 (28.09.2000)

PCT

(10) International Publication Number
WO 00/57184 A3

(51) International Patent Classification[7]: G01N 33/566, 33/569, C07K 5/00, 7/00, C12N 5/00, 15/00, A01K 67/00, C07K 16/00, A61K 38/00, G01N 33/68

(21) International Application Number: PCT/GB00/01024

(22) International Filing Date: 17 March 2000 (17.03.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

9906432.1	19 March 1999 (19.03.1999)	GB
9915075.7	28 June 1999 (28.06.1999)	GB

(71) Applicant *(for all designated States except US)*: **KUDOS PHARMACEUTICALS LIMITED** [GB/GB]; 327 Cambridge Science Park, Milton Road, Cambridge CB4 4WG (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **JACKSON, Stephen, Philip** [GB/GB]; 45 Thornton Road, Girton, Cambridge CB3 0NP (GB). **DUROCHER, Daniel** [GB/GB]; 67 Kingston Street, Cambridge CB1 2NU (GB).

(74) Agents: **WALTON, Seán, M.** et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

(88) Date of publication of the international search report:
8 March 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/57184 A3

(54) Title: SCREENING METHODS BASED ON FHA DOMAINS

(57) Abstract: Assays, screening methods, peptides, mimetics, and methods of use are described which are based on the surprising discovery and characterisation of a direct interaction between the FHA1 domain of the *Sacharomyces cerevisiae* protein Rad53p, and phosphorylated polypeptides. This interaction is relevant to numerous cellular processes which are of interest in therapeutic contexts.

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
G01N 33/566, 33/569, C07K 5/00, 7/00, C12N 5/00, 15/00, A01K 67/00, C07K 16/00, A61K 38/00

A2

(11) International Publication Number: **WO 00/57184**

(43) International Publication Date: 28 September 2000 (28.09.00)

(21) International Application Number: PCT/GB00/01024

(22) International Filing Date: 17 March 2000 (17.03.00)

(30) Priority Data:

9906432.1	19 March 1999 (19.03.99)	GB
9915075.7	28 June 1999 (28.06.99)	GB

(71) Applicant *(for all designated States except US)*: KUDOS PHARMACEUTICALS LIMITED [GB/GB]; 327 Cambridge Science Park, Milton Road, Cambridge CB4 4WG (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: JACKSON, Stephen, Philip [GB/GB]; 45 Thornton Road, Girton, Cambridge CB3 0NP (GB). DUROCHER, Daniel [GB/GB]; 67 Kingston Street, Cambridge CB1 2NU (GB).

(74) Agents: WALTON, Seán, M. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: ASSAYS, METHODS AND MEANS

(57) Abstract

Assays, screening methods, peptides, mimetics, and methods of use are described which are based on the surprising discovery and characterisation of a direct interaction between the FHA1 domain of the *Sacharomyces cerevisiae* protein Rad53p, and phosphorylated polypeptides. This interaction is relevant to numerous cellular processes which are of interest in therapeutic contexts.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01024

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/566 G01N33/569 C07K5/00 C07K7/00 C12N5/00
C12N15/00 A01K67/00 C07K16/00 A61K38/00 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DUROCHER D. ET AL.: "The FHA domain is a modular phosphopeptide recognition motif" MOLECULAR CELL, vol. 4, September 1999 (1999-09), pages 387-394, XP002151809 the whole document ---	1-31, 33-37
X	SUN Z. ET AL.: "Rad53 FHA domain associated with phosphorylated Rad9 in the DNA damage checkpoint" SCIENCE, vol. 281, 10 July 1998 (1998-07-10), pages 272-274, XP002151810 cited in the application the whole document --- -/--	1-31, 33-37

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 November 2000	13/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pellegrini, P

4

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOFMANN K. ET AL.: "The FHA domain: a putative nuclear signalling domain found in protein kinases and transcription factors" TIBS, vol. 20, 1995, pages 347-349, XP002151811 cited in the application figure 1	1-31, 33-37
X	EMILI A.: "MEC1-dependent phosphorylation of Rad9p in response to DNA damage" MOLECULAR CELL, vol. 2, 1998, pages 183-189, XP002151812 cited in the application the whole document	1-31, 33-37
X	VIALARD J.E. ET AL.: "The budding yeast Rad9 checkpoint protein is subjected to Mec1/Tel1-dependent hyperphosphorylation and interacts with Rad53 after DNA damage." THE EMBO JOURNAL, vol. 17, no. 19, 1998, pages 5679-5688, XP002151813 cited in the application the whole document	1-31, 33-37
X	PERICH J.W. ET AL.: "Synthesis of phosphopeptides by the Multipin method: evaluation of coupling methods for the incorporation of Fmoc-Tyr(PO3Bzl,H)-OH, Fmoc-Ser(PO3Bzl,H)-OH and Fmoc-Thr(PO3Bzl,H)-OH" LETTERS IN PEPTIDE SCIENCE, vol. 6, 1999, pages 91-97, XP000961751 abstract page 93, column 2, paragraph 2	1-31, 33-37
X	US 5 763 164 A (CALENOFF EMANUEL) 9 June 1998 (1998-06-09) claim 6	1-31, 33-37
P,X	LI J. ET AL.: "Kinase interaction domain of kinase-associated protein phosphatase, a phosphoprotein-binding domain." PROC. NATL. ACAD. SCI. USA, vol. 96, July 1999 (1999-07), pages 7821-7826, XP002151814 the whole document	1-31, 33-37
P,X	WO 99 42833 A (IMP CANCER RES TECH ;PARKER PETER JOSEPH JACQUES (GB)) 26 August 1999 (1999-08-26) figure 10	1-31, 33-37

4

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 3-4, 6-13, 19-23, 25, 32-37

1) Claims 3-4 relate to FHA domains defined by reference to a desirable characteristic or property, namely being identified by the method of claim 2, i.e. binding to a phosphorylated peptide comprising amino acid sequence Thr(P)-X1-X2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X1 and X2 each represent any amino acid residue.
The claims cover all FHA domains having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for the FHA domains of Rad53.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
A search has been performed on FHA domains belonging to Rad53 protein.

2) Claims 6-13, 19 and 25 relate to phosphopeptides defined by reference to a desirable characteristic or property, namely being identified by a method according to claim 5, i.e. binding to an FHA domain, to their use in screening an FHA domain which binds to them, and to nucleic acid molecules, vectors, host cells and transgenic animals related to these phosphopeptides.
The claims cover all phosphopeptides and related subject-matter having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for phosphopeptides corresponding to the consensus sequence Thr(P)-X1-X1-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X1 and X2 represent any amino acid residue.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
A search has been performed on phosphopeptides corresponding to the above-mentioned consensus sequence, and on all the subject-matter of claims 10-13, 19 and 25 which is related to them.

3) Claims 20-23 relate to compounds defined by reference to a desirable characteristic or property, namely being identified by the method of claim 1, i.e. modulating the binding of an FHA domain to a target phosphopeptide.
The claims cover all substances having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such substances.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
However, a search has been performed on antibodies directed at the FHA domain at positions corresponding to Arg-70 and His-88 of Rad53p, and on antibodies directed at the motif Thr(P)-X1-X2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue and X1 and X2 represent any amino

acid.

Claim 32 relates to mimetics defined by reference to a desirable characteristic or property, namely being identified by the method of claim 31.
The claim covers all mimetics having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such mimetics.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the subject-matter for which protection is sought in claim 32 is impossible.
Consequently, no search has been performed on this claim.

Claims 33-34 relate to the use of a phosphopeptide according to any one of claims 6 to 9, an FHA domain or fragment thereof according to claim 3 or claim 4 or a substance according to any one of claims 21 to 23, in the manufacture of a medicament for the treatment of conditions associated with cellular processes mediated by the binding of an FHA domain to a phosphopeptide, or for the manufacture of a medicament for antipathogen treatment.
Claim 35 relates to pharmaceutical compositions comprising one or more of an FHA domain according to claim 3 or 4, a phosphopeptide according to any one of claims 6 to 9, and a substance according to any one of claims 21 to 23.
A search has been performed on the uses and pharmaceutical compositions based on the subsets of phosphopeptides according to claims 6-9, FHA domains according to claims 3-4 and substances according to claims 21-23 for which a search has been performed, as explained in par. 1-3 of this motivation, and for the same reasons.

6) Claims 36-37 relate to methods of treatment of human body by therapy, based on adiministering the pharmaceutical compositions of claim 35. A search has been performed on the alleged effects of the pharmaceutical compositions for which a search has been performed as explained in par. 5 of this motivation, and for the same reasons.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/01024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5763164 A	09-06-1998	AU 6631494 A	08-11-1994
		CA 2160713 A	27-10-1994
		CN 1125399 A	26-06-1996
		EP 0693931 A	31-01-1996
		JP 8509216 T	01-10-1996
		WO 9423728 A	27-10-1994
WO 9942833 A	26-08-1999	AU 2538899 A	06-09-1999

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SMW/CP5845706		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/01024	17/03/2000	19/03/1999
International Patent Classification (IPC) or national classification and IPC G01N33/566		
Applicant KUDOS PHARMACEUTICALS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18/10/2000	22.05.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bigot-Maucher, C Telephone No. +49 89 2399 7415

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01024

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-75 as originally filed

Claims, No.:

1-37 as originally filed

Drawings, sheets:

1/8-8/8 as originally filed

Sequence listing part of the description, pages:

1-39, filed with the letter of 27.10.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3-4, 6-13, 19-23, 25, 33-37 (all partially), 32 (completely).

because:

☒ the said international application, or the said claims Nos. 36-37 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 3-4, 6-13, 19-23, 25, 33-37 (all partially) and 32 (completely).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-12, 14, 16, 20, 24-27, 30-31,
Inventive step (IS)	Yes:	Claims	
	No:	Claims	13, 15, 17-19, 21-23, 28-29, 33-37
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	1-31, 33-35

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Point II:

The priority of the present application is valid for claims 1-9, 16, 19-20, 24-25, 28-33 and 36. Thus, the intermediate documents "WO-A-99/42833","MOLECULAR CELL, vol. 4, September 1999, pages 387-394" and "PROC. NATL. ACAD. SCI. USA, vol. 96, July 1999, pages 7821-7826" published between the priority dates (P1: 19.3.1999, P2: 28.6.1999) and the filing date (17.3.2000) are not considered to be state of the art and therefore not taken into account for the examination of the above mentioned claims.

However, the priority of claims 10-15, 17-18, 21-23, 26-27, 34-35 and 37 is not valid, since the subject-matter of said claims could not be found in the priority documents. Thus, the document "MOLECULAR CELL, vol. 4, September 1999, pages 387-394" is considered to be state of the art and taken into account for the examination of said claims.

The following technical features could not be found in the priority documents:

claims 10-13:	nucleic acid molecule encoding an "FHA domain according to claim 3 or 4 or a phosphopeptide according to any one of claims 6 to 9"; the priority documents only disclose nucleic acid molecules encoding unphosphorylated polypeptides (see P1, p 16-17, bridging par, or P2, p 18, l 14-15).
claims 14-15:	"test substance"; said general term could not be found in the priority documents
claims 17-18:	the whole claim 17
claim 21-23, 35:	"single chain antibody"
claim 26-27:	"material containing the polypeptide" ; said general term could not be found in the priority documents
claims 34 and 37:	"pathogen"; said general term could not be found in the priority documents

Point III:

1. Claims 36-37 relate to subject-matter considered by this Authority to be covered

by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2. A partial search has been performed on claims 3-4, 6-13, 19-23, 25 and 32-37, since a meaningful search over the whole of the claimed scope was impossible for the following reasons:

- claims 3-4:
  the application only provides support within the meaning of Article 6 PCT and / or disclosure within the meaning of Article 5 PCT for the FHA domains of Rad 53.
- claims 6-13, 19 and 25:
  the application only provides support and / or disclosure for phosphopeptides corresponding to the consensus sequence Thr(P)-X_1-X_2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X_1 and X_2 represent any amino acid residue, and for all the subject-matter of claims 10-13, 19 and 25 which is related to them.
- claims 20-23:
  the application only provides support and / or disclosure for antibodies directed to the FHA domain at positions corresponding to Arg-70 and His-88 of Rad53p, and for antibodies directed to the motif Thr(P)- X_1-X_2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X_1 and X_2 represent any amino acid residue
- claim 32:
  no search has been performed, since the application does not provide any support and / or disclosure for mimetics covered by said claim
- claims 33-37:
  a search has been performed on the uses, pharmaceutical compositions based on the subsets of phosphopeptides according to claims 6-9, FHA domains according to claims 3-4 and substances according to claims 21-23, as well as for the alleged effects of said pharmaceutical compositions for the reasons outlined under the paragraphs here above

Examination was carried out on the searched subject-matter of the above mentioned claims only as well as on the completely searched claims 1-2, 5, 14-18, 24 and 26-31.

Point V:

Reference is made to the following documents:

D1: MOLECULAR CELL,
vol. 4, September 1999 (1999-09), pages 387-394
(only state of the art for claims 10-15, 17-18, 21-23, 26-27, 34-35 and 37)

D2: SCIENCE,
vol. 281, 10 July 1998 (1998-07-10), pages 272-274, cited in the application

D4: MOLECULAR CELL,
vol. 2, 1998, pages 183-189, cited in the application

D5: THE EMBO JOURNAL,
vol. 17, no. 19, 1998, pages 5679-5688, cited in the application

D6: LETTERS IN PEPTIDE SCIENCE,
vol. 6, 1999, pages 91-97

1. Novelty and Inventive Step

1.1. **Independent claims 1-2, 5 and 24-25 do not appear to be novel** (Article 33(2) PCT) in the light of D2, D4 or D5:

D2 discloses the effect of the use of DNA damaging agents such as MMS and HU (test substances) (p 273, 1st col, 1st full par) on Rad9 (phosphopeptide) and Rad53 (FHA domain) coupling (i.e. binding). The FHA2 domain of Rad53 functions as a specific modular protein-binding unit, the function of which is modified by phosphorylation (p 274, 2nd col, 1st full par). Rad9 is phosphorylated after DNA damage (abstract). D2 shows that Rad9 and Rad53 coimmunoprecipitate (determination of binding; see present application, p 39, l 21) after DNA damage (p 273, 1st to 2nd col, bridging par). GST-pull down assays reveal the same result (fig. 1(C)) (determination of binding; see present application, p 40, l 2 ff.).

D4 already discloses that DNA damage-modified Rad9p forms a stable complex with Rad53p in vivo (p 184, 1st col, 1st par). Different DNA damaging agents (test substance) were given to the cells. Rad53p and Rad9 present in the cell extracts

could be coimmunoprecipitated (determination of binding) either with an anti-Rad53p or with anti-Rad9p antibody. Said coimmunoprecipitation only occurred after DNA damage, i.e. after the addition of the DNA damaging agent, which resulted in Rad53p phosphorylation (p 186, 2nd col, last full par and last sentence).

D5 describes that Rad9 physically associates (i.e. binds) with Rad53 after DNA damage. A DNA damaging agent is given to the cells, for instance methyl methane sulfonate (abstract). Affinity purification of Rad9 co-purifies (determination of binding) Rad53 (p 5684, 1st col, full par).

1.2. **The same applies to dependent claims 14** (D2, fig. 2: endogenous Rad9 and Rad53) **and 16** (D5, p 5684, 1st col, full par), which only disclose subject-matter well-known in the art.

1.3. **Claim 15 is novel** (Article 33(2) PCT) in the light of D2, D4 or D5, since none of the documents discloses the quantification of the phosphopeptide, FHA domain or test substance.

However, the additional feature of said dependent claim is purely conventional and does not lead to an unexpected effect. Thus, **claim 15 is not considered inventive** (Article 33(3) PCT).

1.4. **Claims 17-19 are considered novel** (Article 33(2) PCT), since none of the available prior art documents discloses the claimed subject-matter.

However, the additional features of said dependent claims are purely conventional and does not seem to lead to an unexpected effect. Therefore, **claims 17-19 do not appear to be inventive** (Article 33(3) PCT).

1.5. **Claims 3-4 and 7 do not appear to be novel** (Article 33(2) PCT) in the light of D2 assuming that Rad9 possesses the disclosed amino acid sequence - Thr(P)-X_1-X_2-Asp-: thus, one embodiment of said claim is Rad53 (which possesses a FHA domain; see present application, p23, l 29-31) binding to Rad9:

D2 already reveals that Rad53 of S. cerevisiae has a FHA domain and couples with the phosphorylated phosphopeptide Rad9. FHA appears to be a protein-binding domain (abstract). Thus, said document already teaches the Rad9 / Rad53 binding via FHA of Rad53.

Claims 3 and 7 are furthermore not considered novel (Article 33(2) PCT) in the light of D6, which discloses a phosphopeptide comprising the amino acid sequence -Thr(P)-X_1-X_2-Asp- (abstract).

1.6. The subject-matter of **claims 6 and 8 is not novel** (Article 33(2) PCT) in the light of D2.

D2 already discloses the binding of phosphorylated Rad9 to Rad53 via the latter's FHA domain (abstract).

1.7. Assuming that Rad9 comprises one of the amino acid sequences shown in figure 2, then D2 is **novelty destroying** (Article 33(2) PCT) **for claim 9**.

1.8. The subject-matter of **claims 10-12 is not considered novel** (Article 33(2) PCT) in the light of D1 or D2:

D1 teaches the manufacture of FHA1 and FHA2 encoding DNA by PCR using particular primers and the subsequent cloning into the vector pGEX- 4T3 (p 393, 1st col, 4th par).
D2 describes TWY397 host cells carrying the vector pRS316 containing RAD9-FLAG DNA (fig. 2(A)). RAD9-FLAG DNA encodes the protein Rad9 followed by a single epitope tag (fig. 1). Furthermore, mutant and wild type FAH2 alleles were introduced into the vector pRS316, which was then introduced into DZ424 cells (fig. 4(A)).

1.9. The subject-matter of **claim 13 appears to be novel** (Article 33(2) PCT) in the light of the available prior art, since none of the documents discloses a transgenic animal.

Claim 13 is however not considered inventive (Article 33(3) PCT), since it is

common to provide a transgenic animal comprising a specific nucleic acid. Such a procedure is well-known in the art.

1.10. The subject-matter of **claim 20 is not considered novel** (Article 33(2) PCT) in the light of D2 (p 273, 1st col, l 8-9), D4 (p 184, 1st col, 3rd par) or D5 (fig. 1), since said documents already disclose modulating substances such as HU, MMS and 4-NQO.

1.11. The subject-matter of dependent claims 21-23 is considered novel (Article 33(2) PCT), since none of the available prior art documents discloses the claimed antibody.

The subject-matter of **claims 21-23 is not considered inventive** (Article 33(3) PCT) for the following reasons. The production of antibodies against a known protein is well-established in the art. Furthermore, it is common in the art to use antibodies for modulating the binding of substances.

1.12. The subject-matter of independent claims 26-27 does not appear to be novel (Article 33(2) PCT) in the light of D5, p 5684, 1st col, full par. D5 already discloses the purification of Rad53 and Rad9 (see also Fig. 7).

1.13. The subject-matter of **independent claims 28-29 is novel** (Article 33(2) PCT) in the light of D5, since the provision of a mimetic for the phosphopeptide is not disclosed.

The provision of mutant phosphopeptides analogous to the mutants of the FHA domain is however not considered inventive according to Article 33(3) PCT (see 1.14.). Thus **claim 28 does not comply with the requirements of Article 33(3) PCT**.

The subject-matter of **dependent claim 29 is not considered inventive** (Article 33(3) PCT)(see 1.14.), since it is not apparent which surprising technical effect arises from the claimed amino acid sequences.

1.14. The subject-matter of independent claims 30-31 does not appear to be novel (Article 33(2) PCT) in the light of D2, since said document already discloses a

method for localizing sequences necessary for Rad9-Rad53 interaction. Several Rad53 mutants (mimetics) are made, and their binding activity to Rad9 is measured. One of them has full binding activity (p 273, 2nd col to 5th col).

1.15. The subject-matter of **claims 33-37 appears to be novel** (Article 33(2) PCT) in the light of the available prior art, since none of the documents discloses the therapeutic use of the phosphopeptide or the FHA domain.

However, the use of the phosphopeptide or FHA domain in a therapeutical treatment does not appear to be inventive in the light of D1, p 393, 1st col, last sentence. Said passage already suggests such therapeutic use, and the skilled person would know how to make a medicament as well as how to administer the phosphopeptide or FHA domain. Thus, the subject-matter of **claims 34-35 and 37 is not considered inventive** according to Article 33(3) PCT.

The subject-matter of **claims 33 and 36 does not appear inventive** (Article 33(3) PCT) either, since the prior art clearly describes the activation of Rad9 and Rad53 due to DNA damage in DNA repair mechanisms (see for instance D2, p 272, 1st col, 1st par). The use of these substances as therapeutics in disorders relating to DNA repair is therefore considered obvious.

2. Industrial Applicability

For the assessment of the present claims 36-37 on the question whether they are industrially applicable, no unified criteria exist in the PCT contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Point VI:

The subject-matter of the interfering document "MOLECULAR CELL, vol. 4, September 1999, pages 387-394" refers to relevant subject-matter.

The above documents are published after the present application's priority date, but before its filing date and are therefore relevant for those parts of the present application, if any, which do not have a valid claim to priority (see Point II herein above).

Point VII:

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D6 is not mentioned in the description, nor are these documents identified therein.

Point VIII:

1. Lack of clarity of the claims as a whole arises, since the plurality of independent (23 independent claims in a total of 37 claims!) claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.

   Hence, claims 1-37 do not meet the requirements of Article 6 PCT.

   No amended set of claims has been filed defining the relevant subject-matter in terms of a minimum number of independent claims in each category followed by dependent claims covering features which are merely optional (Rule 6.4 PCT).

2. Claim 9 does not comply with Rule 6.1(a) PCT, since it contains a reference to figure 2. Claims shall not rely, in respect of the technical features of the invention, on references to the description or drawings.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
SMW/CP5845706		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/01024	17/03/2000	19/03/1999
Applicant		
KUDOS PHARMACEUTICALS LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[X] furnished subsequently to this Authority in written form.

[X] furnished subsequently to this Authority in computer readble form.

[X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

SCREENING METHODS BASED ON FHA DOMAINS

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 3-4, 6-13, 19-23, 25, 32-37

1) Claims 3-4 relate to FHA domains defined by reference to a desirable characteristic or property, namely being identified by the method of claim 2, i.e. binding to a phosphorylated peptide comprising amino acid sequence Thr(P)-X1-X2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X1 and X2 each represent any amino acid residue. The claims cover all FHA domains having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for the FHA domains of Rad53.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
A search has been performed on FHA domains belonging to Rad53 protein.

2) Claims 6-13, 19 and 25 relate to phosphopeptides defined by reference to a desirable characteristic or property, namely being identified by a method according to claim 5, i.e. binding to an FHA domain, to their use in screening an FHA domain which binds to them, and to nucleic acid molecules, vectors, host cells and transgenic animals related to these phosphopeptides.
The claims cover all phosphopeptides and related subject-matter having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT only for phosphopeptides corresponding to the consensus sequence Thr(P)-X1-X1-Asp, wherein Thr(P) denotes a phosphorylated threonine residue, and X1 and X2 represent any amino acid residue.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
A search has been performed on phosphopeptides corresponding to the above-mentioned consensus sequence, and on all the subject-matter of claims 10-13, 19 and 25 which is related to them.

3) Claims 20-23 relate to compounds defined by reference to a desirable characteristic or property, namely being identified by the method of claim 1, i.e. modulating the binding of an FHA domain to a target phosphopeptide.
The claims cover all substances having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such substances.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
However, a search has been performed on antibodies directed at the FHA domain at positions corresponding to Arg-70 and His-88 of Rad53p, and on antibodies directed at the motif Thr(P)-X1-X2-Asp, wherein Thr(P) denotes a phosphorylated threonine residue and X1 and X2 represent any amino

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

acid.

Claim 32 relates to mimetics defined by reference to a desirable characteristic or property, namely being identified by the method of claim 31.
The claim covers all mimetics having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such mimetics.
In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the subject-matter for which protection is sought in claim 32 is impossible.
Consequently, no search has been performed on this claim.

Claims 33-34 relate to the use of a phosphopeptide according to any one of claims 6 to 9, an FHA domain or fragment thereof according to claim 3 or claim 4 or a substance according to any one of claims 21 to 23, in the manufacture of a medicament for the treatment of conditions associated with cellular processes mediated by the binding of an FHA domain to a phosphopeptide, or for the manufacture of a medicament for antipathogen treatment.
Claim 35 relates to pharmaceutical compositions comprising one or more of an FHA domain according to claim 3 or 4, a phosphopeptide according to any one of claims 6 to 9, and a substance according to any one of claims 21 to 23.
A search has been performed on the uses and pharmaceutical compositions based on the subsets of phosphopeptides according to claims 6-9, FHA domains according to claims 3-4 and substances according to claims 21-23 for which a search has been performed, as explained in par. 1-3 of this motivation, and for the same reasons.

6) Claims 36-37 relate to methods of treatment of human body by therapy, based on adiministering the pharmaceutical compositions of claim 35. A search has been performed on the alleged effects of the pharmaceutical compositions for which a search has been performed as explained in par. 5 of this motivation, and for the same reasons.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01024

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/566 G01N33/569 C07K5/00 C07K7/00 C12N5/00
C12N15/00 A01K67/00 C07K16/00 A61K38/00 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DUROCHER D. ET AL.: "The FHA domain is a modular phosphopeptide recognition motif" MOLECULAR CELL, vol. 4, September 1999 (1999-09), pages 387-394, XP002151809 the whole document ---	1-31, 33-37
X	SUN Z. ET AL.: "Rad53 FHA domain associated with phosphorylated Rad9 in the DNA damage checkpoint" SCIENCE, vol. 281, 10 July 1998 (1998-07-10), pages 272-274, XP002151810 cited in the application the whole document --- -/--	1-31, 33-37

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 November 2000	13/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pellegrini, P

4

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01024

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOFMANN K. ET AL.: "The FHA domain: a putative nuclear signalling domain found in protein kinases and transcription factors" TIBS, vol. 20, 1995, pages 347-349, XP002151811 cited in the application figure 1	1-31, 33-37
X	EMILI A.: "MEC1-dependent phosphorylation of Rad9p in response to DNA damage" MOLECULAR CELL, vol. 2, 1998, pages 183-189, XP002151812 cited in the application the whole document	1-31, 33-37
X	VIALARD J.E. ET AL.: "The budding yeast Rad9 checkpoint protein is subjected to Mec1/Tel1-dependent hyperphosphorylation and interacts with Rad53 after DNA damage." THE EMBO JOURNAL, vol. 17, no. 19, 1998, pages 5679-5688, XP002151813 cited in the application the whole document	1-31, 33-37
X	PERICH J.W. ET AL.: "Synthesis of phosphopeptides by the Multipin method: evaluation of coupling methods for the incorporation of Fmoc-Tyr(PO3Bzl,H)-OH, Fmoc-Ser(PO3Bzl,H)-OH and Fmoc-Thr(PO3Bzl,H)-OH" LETTERS IN PEPTIDE SCIENCE, vol. 6, 1999, pages 91-97, XP000961751 abstract page 93, column 2, paragraph 2	1-31, 33-37
X	US 5 763 164 A (CALENOFF EMANUEL) 9 June 1998 (1998-06-09) claim 6	1-31, 33-37
P,X	LI J. ET AL.: "Kinase interaction domain of kinase-associated protein phosphatase, a phosphoprotein-binding domain." PROC. NATL. ACAD. SCI. USA, vol. 96, July 1999 (1999-07), pages 7821-7826, XP002151814 the whole document	1-31, 33-37
P,X	WO 99 42833 A (IMP CANCER RES TECH ;PARKER PETER JOSEPH JACQUES (GB)) 26 August 1999 (1999-08-26) figure 10	1-31, 33-37

4

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/01024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5763164 A	09-06-1998	AU 6631494 A	08-11-1994
		CA 2160713 A	27-10-1994
		CN 1125399 A	26-06-1996
		EP 0693931 A	31-01-1996
		JP 8509216 T	01-10-1996
		WO 9423728 A	27-10-1994
WO 9942833 A	26-08-1999	AU 2538899 A	06-09-1999

PATENT COOPERATION TREA . .

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 November 2000 (20.11.00)	
International application No. PCT/GB00/01024	**Applicant's or agent's file reference** SMW/CP5845706
International filing date (day/month/year) 17 March 2000 (17.03.00)	**Priority date** (day/month/year) 19 March 1999 (19.03.99)
Applicant JACKSON, Stephen, Philip et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

18 October 2000 (18.10.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Pascal Piriou
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

GB0001024

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		